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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/625,307	07/23/2003	Julia Elizabeth Thompson	05569.0007.CPUS02	2383

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Prosecution
Howrey Simon Arnold & White, LLP
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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/625,307	THOMPSON ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *6-12 and 24-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,13-23 and 34-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09054847.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 11/13/06, has been entered.

Claims 27, 29, 32 and 34-39 have been amended.

Claims 1-39 are pending.

Applicant's election of the species corresponding to the 6B1 antibody, which comprises SEQ. ID. NOS. 6 and 43, for prosecution on the merits to which the claims shall be restricted, if no generic claim if finally held to be allowable (see Election, filed 11/13/06).

Claims 1-5, 13-23 and 34-39 are being acted upon as they read on the elected species.

Claims 6-12 and 24-33 have been withdrawn from prosecution as being drawn to non-elected species.

2. Applicant's Preliminary Remarks, in conjunction with Roberts 132 Declaration and Exhibits, filed 7/23/03 and 11/23/04 are acknowledged.

With respect to priority, it appears that applicant's earliest U.S. priority date is that of PCT/GB96/02450, filed 10/7/1996 (see Section 3 below).

With respect to assertions about the prior art rejections set forth in the priority USSNs, it is noted that the grounds of rejection set forth herein differ. Therefore, applicant's remarks are acknowledged, however they do not address the rejections set forth herein.

3. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Applicant should amend the first line of the specification to update the status (and relationship) of the priority documents.

With respect to priority, it appears that applicant's earliest U.S. priority date is that of PCT/GB96/02450, filed 10/7/1996.

4. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required

5. The following is a quotation of the first paragraph of 35 U.S.C. § 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-5, 13-23 and 34-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

It has been well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. All of the heavy and light chain CDRs should be in their proper order and in the context of framework sequences which maintain their required conformation in order to provide a binding molecule having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites.

Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 79: 1979-1983 (1982). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. Single amino changes to either a CDR or even in certain circumstances to the framework can result in decrease affinity of antigen or even ablation of antibody binding and specificity. Also, see Colman, Research in Immunology 145: 33-36, 1994.

It is unlikely that any "part of a VH domain encoded by a germ line gene segment or a rearranged gene segment", "part of either a VL kappa domain or a VL lambda domain" or the polypeptides (antibodies) specific for TGF-β which do not comprise all six (6) CDRs broadly encompassed by the claimed invention as defined by the claims will have the required binding function for TGF-β, encompassed by the claimed invention.

Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the instant disclosure alone. One of skill in the art would neither expect nor predict the appropriate functioning of the claimed CD154-specific binding polypepties (antibodies) as broadly as is claimed. Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

Without sufficient guidance, the changes which can be made in the structure of the claimed TGFβ-specific binding polypeptides / antibodies and still provide or maintain sufficient or the claimed activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Applicant is invited to amend the claims to limit the TGFβ-binding polypeptides / antibodies to the particular SEQ IDS NOS. that define the instant TGFβ –specific antibodies (e.g., the elected 6B1 antibody) disclosed in the specification as filed in order to obviate this rejection.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-5 are rejected under 35 U.S.C. § 102(b) as being anticipated by Griffiths et al. (WO 93/11236) (see entire document).

Griffiths et al. teach the production of anti-self antibodies, including antigen-binding fragments thereof (e.g., ScFv) (e.g. see page 2, paragraph 1), from phage libraries as a powerful way of obtaining diagnostic and therapeutic antibodies and avoiding the antigenicity of foreign antibodies (e.g., mouse antibodies) (e.g., see page 1) (See entire document). Among the Applications of Antibodies to Self Antigens (e.g., see pages 24-31). Griffiths et al. teach antibodies that modify the action of self molecules such as growth factors, including TGF-β (e.g., see pages 24- 31 including Human Antibodies Against Cytokines on page 27). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced antibodies to TGF-β.

10. Claims 1-5 are rejected under 35 U.S.C. § 102(e) as being anticipated by Griffiths et al. (U.S. Patent No. 5,962,255) (1449; #A2) (see entire document).

Griffiths et al. teach the production of anti-self antibodies, including antigen-binding fragments thereof (e.g., ScFv) (e.g. see column 8, paragraph 1), from phage libraries as a powerful way of obtaining diagnostic and therapeutic antibodies and avoiding the antigenicity of foreign antibodies (e.g., mouse antibodies) (see entire document). Among the self antigen, Griffiths et al. teach antibodies that modify the action of self molecules such as cytokines (e.g., see Table 2), including TGF-β (e.g., see Example 4 on columns 48-52). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced antibodies to TGF-β.

11. Claims 1-5 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lucas et al. (J. Immunol. 145: 1415-1422, 1990) AND/OR
over Dasch et al. (U. S. Patent 5,571,714) AND/OR
over Iwata et al. (U.S. Patent No. 5,262,319)
in view of Griffiths et al. (WO 93/11236) or Griffiths et al. (U.S. Patent No. 5,962,255))
(1449; #A2).

Lucas et al. teach the generation of TGF-β-specific antibodies, including neutralizing antibodies, that could be useful to regulate immune functions, including therapeutic regimens (see entire document, including Abstract and Discussion).

Dasch et al. teach TGF-β-specific antibodies and antigen-binding fragments thereof, which can be used for a number of utilities, including neutralizing the biological activity of TGF-β in the treatment of diseases (e.g., see entire document, including Modes of Carrying Out the Invention). In addition, Dasch et al. teach the use of chimeric antibodies (e.g., see column 2, lines 50-55), as an early means of decreasing the immunogenicity of therapeutic antibodies in treating humans. Also, the use of human immunoglobulin elements (e.g., Fc domains) were known to provide human immunoglobulin effector function to recombinant antibodies of interest at the time the invention was made.

Iwata et al. teach TGF-β-specific antibodies and antigen-binding fragments thereof, which can be used for a number of utilities, including neutralizing the biological activity of TGF-β in the treatment of diseases (e.g., see entire document, including Detailed Description of the Invention). In addition, Iwata et al. teach the use of recombinant technology to engineer antibodies that made non-immunogenic in humans (e.g. see column 6, paragraph 4)

The primary references differ from the claimed invention by not describing the known method of producing human antibodies to self-antigens at the time the invention was made.

Both Griffiths et al. references teach and provide motivation to produce human antibodies to self-antigens, including cytokines such as TGF-β from phage libraries to self-antigen by the ordinary artisan at the time the invention was made.

Griffiths et al. (WO) teach the production of anti-self antibodies, including antigen-binding fragments thereof (e.g., ScFv) (e.g. see page 2, paragraph 1), from phage libraries as a powerful way of obtaining diagnostic and therapeutic antibodies and avoiding the antigenicity of foreign antibodies (e.g., mouse antibodies) (e.g., see page 1) (See entire document). Among the Applications of Antibodies to Self Antigens (e.g., see pages 24- 31). Griffiths et al. teach antibodies that modify the action of self molecules such as growth factors, including TGF-β (e.g., see pages 24- 31 including Human Antibodies Against Cytokines on page 27).

Griffiths et al. (U.S.) teach the production of anti-self antibodies, including antigen-binding fragments thereof (e.g., ScFv) (e.g. see column 8, paragraph 1), from phage libraries as a powerful way of obtaining diagnostic and therapeutic antibodies and avoiding the antigenicity of foreign antibodies (e.g., mouse antibodies) (see entire document). Among the self antigen, Griffiths et al. teach antibodies that modify the action of self molecules such as cytokines (e.g., see Table 2), including TGF-β (e.g., see Example 4 on columns 48-52).

Employ either human or humanized antibodies that may differ from those provided by the phage display libraries, taught by Marks et al.; it was clear that the ordinary artisan would have employed human antibodies to antigens of interest, including self-antigens such as TGF-β, in a variety of immunological procedures, including diagnostic assays, at the time the invention was made.

The primary and secondary references provide clear motivation for the use of anti-human TGF-β antibodies for a variety of procedures (see above). One of ordinary skill in the art would have been motivated to apply the use of phage libraries to produce anti-human TGF-β antibodies in a variety of procedures, including therapeutic regimens to produce human antibodies and antigen-binding fragments thereof that take advantage of decreased immunogenicity of human therapeutic antibodies in therapeutic regimens of treating humans as well as taking advantages of human immunoglobulin effector functions, if desired. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success in view of the teachings of Griffiths et al. (WO and U.S.) at the time the invention was made. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); In re Van Ornam, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and In re Goodman, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR § 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR § 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR § 3.73(b).

13. Claims 1-5 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,492,497.

Although the recitation of the instant and patented claims differs, the patented claims, drawn to TGF-β-specific antibodies (binding members) anticipate the generic TGF-β-specific antibodies of the instant invention.

14. As pointed out previously in parent USSNs, claims drawn to the specific TGF-β-specific antibodies, such as the elected 6B1 antibody, appear to be free of the prior art and in condition for allowance.

However, applicant should amend the claims to recite the SEQ ID NOS. that define a complete antibody comprising all six (6) CDRs to be compliant with 35 USC 112, first paragraph, enablement.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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